UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/595,620 | 05/01/2006 | Hyun-Soo Kim | Q94674 | 3640 |

23373 7590 04/29/2008

SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

| EXAMINER | |
|---|---|
| SAJJADI, FEREYDOUN GHOTB | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1633 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 04/29/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/595,620 | KIM ET AL. | |
| | Examiner | Art Unit | |
| | FEREYDOUN G. SAJJADI | 1633 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4 and 6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/1/06; 7/26/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Claims 1-4 and 6 are pending in the application and are under current examination.

### *Information Disclosure Statement*

The information disclosure statement filed 5/1/2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been fully considered, since none of the foreign patent documents, or non-patent literature references were present in the instant application. Applicant is required to provide copies of the missing references to be considered by the examiner.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 6 are rejected under 35 U.S.C. §103(a) as being unpatentable over Furcht et al. (U.S. Patent No.: 7,015,037; effective filing date: Aug. 5, 1999), in view of Kokuzawa et al. (U.S. Patent Application Publication No.: 2006/0134078; effective filing date: Dec. 2, 2002).

The claims embrace a method of differentiating and proliferating a mesenchymal stem cell into a neural cell comprising the steps of: (1) confluent culturing the mesenchymal stem cell

as a pretreatment, and (2) culturing a mesenchymal stem cell in a medium comprising an epithermal growth factor (EGF) and a hepatocyte growth factor (HGF).

Furcht et al. describe the isolation of a sub-population of mesenchymal stem cells from bone marrow mononuclear cells and culturing in media supplemented with various growth factors (the cells are referred to as multipotent adult stem cells; MASC; column 7, lines 1-7; column 14, lines 57-60; column 44, Example 1; limitation of claim 6). The bone marrow mesenchymal cells are further described as able to differentiate into various cells types, including glial and neuronal cells following culture and induction with various factors that included 0.5-100 ng/ml EGF (column 49, Example 5; limitation of claims 1- 3). Furcht et al. separately describe differentiation media comprising both EGF (0.5-100 ng/ml) and HGF (0.5-1000 ng/ml) for the differentiation of epithelial and endodermal cells (column, 52, Example 7, lines 47-50; limitation of claims 2 and 3). Furcht et al. further describe a number of culture conditions where the MASCs are cultured to confluence prior to differentiation with the growth factors. For example, "Differentiation to any muscle phenotype required that MASCs be allowed to become confluent prior to induction of differentiation" (column 21, lines 10-12; limitation of claim 1, step 1); where a sole cytokine was added to confluent MASC maintained in serum free MASC medium for 14 days (column 47, lines 9-10; limitation of claim 4). Stromal differentiation is further described wherein confluent MASC cultures were treated with hepatocytes growth factor and KGF, for 14 days (column 48, lines 1-2).

Furcht et al. do not describe confluent culturing for about 24 hours, or for about 1 to about 50 hours prior to addition of growth factors for differentiation. It should be noted that such culturing periods are within the scope of routine experimentation and optimization in the prior art. Applicants should further note that as indicated in MPEP 2144.05: Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). The non-criticality of the period for confluent culture is evident by the 50 fold difference in the time instantly claimed.

While Furcht et al. do not describe using the combination of EGF and HGF to differentiate the mesenchymal stem cells into neural cells, such combination for neuronal differentiation was known in the prior art of Kokuzawa et al., in describing a medium containing HGF and EGF inducing neurosphere formation from neural stem cells (Abstract; limitation of claim 1, step 2). With regard to the limitation of claim 4, wherein the mesenchymal stem cell is cultured for about 2 weeks in the differentiation medium comprising EGF and HGF, and then HGF is removed, Kokuzawa et al. describe culture comparisons between differentiation media in the presence of EGF, with or without HGF (Fig. 3b and ¶ [0031], p. 3). It is again noted that such alterations in the composition of differentiation media and culture time were considered routine experimentation in the prior art of cell culture.

Both Furcht et al. and Kokuzawa et al. describe the differentiation of stem cells into neuronal cells, and both utilized media comprising EGF and HGF for stem cell differentiation. Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art to combine their respective teachings, to use a neuronal differentiation medium comprising the combination of EGF and HGF, as described by Kokuzawa et al., to differentiate the mesenchymal stem cells of Furcht et al., with a reasonable expectation of success, at the time of the instant invention. A person of skill in the art would be motivated to substitute a differentiation medium containing both EGF and HGF for one containing EGF and various other growth factor, as a matter of design choice, said design choice amounting to combining prior art elements according to known methods to yield predictable results. Applicants should note that the *KSR* case forecloses the argument that a specific teaching, suggestion, or motivation is required to support a finding of obviousness. *KSR International Co. v. Teleflex Inc.*, 550 U.S.-, 82USPQ2d 1385 (2007).

***Conclusion***

**Claims 1-4 and 6 are not allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633